

## Is Irritable Bowel Syndrome A Significant Comorbid Disorder Among Patients With Tension Type Headache?

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### الخلاصة:

**الهدف والخلفية العلمية:** إن العلاقة المرضية بين الصداع التشنجي والإمراض الأخرى هو موضوع اهتمام الباحثين، في الوقت الحاضر لا يوجد دراسة سريرية تحليلية لتوضيح العلاقة المرضية بين الصداع التشنجي ومرض تهيج القولون.

**طريقة البحث:** شملت هذه الدراسة العينية المستقبلية المقارنة، ٣٦٠ مريض يعانون من صاع تشنجي: ٢٠٠ من الإناث و١٦٠ من الذكور من اللذين يعانون من صاع تشنجي تم تشخيصهم اعتماداً على صفات محددة من قبل الجمعية العالمية للصداع (IHS) وتم دراسة نسبة انتشار مرض تهيج القولون بينهم (اعتمد التشخيص IBS على صفات روم ٢ وروم ٣ المعتمدة لدى الجمعية الانكليزية والأمريكية لإمراض الجهاز الهضمي) وتم مقارنة ذلك مع مجموعة مقارنة من اللذين لا يعانون من إي مرض وهم متشابهي الأعمار والأجناس تقريباً إلى المجموعة المصابة بالصداع التشنجي ، ثم تحليل النتائج بالنسبة إلى العمر والجنس ونوع الصداع التشنجي المزمن والحدوث اعتماداً على معادلات إحصائية مستخدمين معادلة الكاي سكوير (X2) ومعدل الاحتمالية ذات القيمة العالية عندما تكون قيمة أقل من 0,05 .

**النتائج:** أوضحت هذه الدراسة إن الصداع التشنجي أكثر شيوعاً في الإناث عنه في الذكور ومعدل الإناث إلى الذكور ٢٥، ١ : ١ ، إن الأعمار المتأثرة بالمرض كانت بين ٢٠-٦٠ سنة لكن الفرق لم يكن إحصائياً ذات قيمة عالية . إن المهم في هذه الدراسة كان هناك قيمة إحصائية عالية (P less than 0.05) لانتشار تهيج القولون بين اللذين يعانون من الصداع التشنجي (٧٩,٧ %) مقارنة بالمجموعة المقارنة ( ١٠ %) وهذه القيمة الإحصائية هي عالية ومهمة بين اللذين يعانون من الصداع التشنجي المزمن ( ٩٣/٣ %) على اللذين يعانون من الصداع التشنجي الحاد ( ٧٢,٩ %). إن النسبة كانت أعلى في الإناث ( ٦٢، ٧ %) عن الذكور ( ٣٧، ٣ %) والأعمار المتأثرة كانت من ٣٠ - ٥٠ لكن لم تكن ذات قيمة إحصائية (p=0.785) بالمقارنة مع بقية الأعمار.

**الاستنتاج:** هنالك علاقة مرضية ذات قيمة إحصائية عالية بين الصداع المزمن وتهيج القولون وهي مهمة من الناحية التشخيصية والعلاجية ، هذه العلاقة تحتمل وجود علاقة مرضية فسلجية مشتركة بينهما و تحتاج إلى توضيح بواسطة بحوث مستقبلية.

**Abstract:**

**Background and aim:** Comorbidity between tension type headache TTH and other disorders is a topic of interest. At the present time, no study examine comorbidity of irritable bowel syndrome (IBS) with TTH as separate entity ; presence of such association have great impact in diagnosis and management of TTH patients for which this prospective cross sectional comparative controlled study have been conducted.

**Methodology:** In this Cross Sectional Controlled Comparative Study , 360 patients ;200 female and 160 male ; age ranges from 15-60 years with diagnosis of TTH depending on International Headache Society (IHS) criteria have been enrolled and compared with age and gender matched 200 controlled individuals ; 116 female and 84 male . The prevalence of IBS (diagnosis made depending on symptoms based criteria Rome II and III criteria) among 2 group were estimated with further evaluation of IBS prevalence made in relation to age , gender and type of TTH ; Statistical analysis done by means of person Chi-square tests with P value < 0.05 was used as a level of significance.

**Results:** TTH is more common in woman , with female to male ratios of 1.25:1, TTH affecting age peaks between 20 and 60 years. There was significant high prevalence of IBS among TTH group versus control healthy group (79.7%, 10% respectively; p value was 0.0001 ) with very high significant prevalence among chronic TTH versus episodic TTH (93.3%, 72.9% respectively ; p value was 0.000056). The prevalence of IBS among TTH group was more common among female versus male (62.7%, 37.3% , respectively).The age peak affected was among thirties and forties ( 29.6% and 28.6% respectively): the sex and gender differences were not significant statistically .

**Conclusion:** patients with TTH have significant associations with IBS as comorbid disorder, such relationships is important from diagnostic and therapeutic point of view . Strength of this association suggests a common pathophysiologic mechanisms which needs further evaluation in future.

**Key words:** Tension type headache, comorbidity, irritable bowel syndrome.

**Introduction**

Headache is a very pervasive symptom and definitely the most common problem encountered by neurologists in daily clinical practice. It affects an estimated 60-80% of Americans at any point in time <sup>1</sup>. The history of headache can be traced back almost to the beginning of the history of mankind from the dawn of civilization <sup>1,2</sup>. The first description of headache dates back to the third millennium BC <sup>2</sup>. Headache has been extensively written since the time of the Babylonian and Sumerian civilization with earliest published reference is a Sumerian epic poem <sup>1,3</sup>. For clinical purposes, The International Headache Society (IHS) has published its revised International Classification of Headache Disorders which are available online ([www.i-h-s.org/](http://www.i-h-s.org/)). There are focuses into 2 broad categories of headaches; primary (headaches with no organic or structural etiology) and secondary (there is underlying structural or organic disease) <sup>4-7</sup>. Life time prevalence study of various headache disorder by Rasmussen's group showed that tension type headache(TTH) was a far more common primary headache than migraine<sup>8</sup>. Estimated prevalence of TTH have varied widely. In western ,one year prevalence ranges from 28 to 63% in men and 34 to 86% in women<sup>8-10</sup>, few TTH prevalence studies done outside western and Arabian world ,Wong et al found very low prevalence in mainland of china <sup>11,12</sup>; unfortunately ,the prevalence of TTH among Iraqi's is unknown.

Migraine comorbidity is well recognized with a number of neurological and psychiatric disorder including stroke, epilepsy ,depression and anxiety disorder<sup>13-17</sup>; few studies were conducted about comorbidity of TTH, which is reported in 52% of patients with fibromyalgia and in 84% of depressed patients as an association<sup>18- 20</sup>.

Comorbidity between headache and other disorders such as psychological or memory problems is a topic of increasing scientific interest to many. The association of TTH and irritable bowel syndrome (IBS) is mentioned as members of dysregulation spectrum syndrome DSS with others entities including fibromyalgia, chronic fatigue syndrome CFS, migraine and restless leg syndrome<sup>21-23</sup>.

At the present time, no previous study has set out to examine comorbidity of irritable bowel syndrome (IBS) with tension type headache TTH definitively ; presence of such association have great impact in diagnosis and management of TTH patients for which this prospective cross sectional comparative controlled study have been conducted.

### **Methodology**

This cross sectional controlled comparative study carried out at middle Euphrates neuroscience center in Annajaf city which is about 160 km southwest to capital Baghdad in period between Jan. 2008 to Feb. 2009. A total of 360 patients were enrolled in this study who met all criteria for diagnosis of tension type headache TTH according to International Headache Society's International Classification of Headache Disorders, 2<sup>nd</sup> Edition (ICHD-2)<sup>24-27</sup>. Among study group; 200 patients were female and 160 were males. The age range was between 15-60 years. A total of 200 healthy control individuals were enrolled as control group, whom are age and gender matched to study group ; 116 patients were female and 84 were male.

All patients in study and control group have been evaluated by gastroenterologist for presence of irritable bowel syndrome (IBS) symptoms with exclusion of organic cause; all patients was interviewed with special questionnaire form for any unspecific abdominal pain or discomfort that recurs , infrequent bowel movements with periods of increased or decreased activity, alleviation of pain and discomfort with defecation, and onset of symptoms with changes in stool frequency and appearance. These are the symptoms which are most frequently employed in making IBS diagnosis in conjunction with the Rome II and new Rome III criteria ; which have been established by British Society of Gastroenterology, the American College of Gastroenterology, and the American Gastroenterological Association<sup>28-30</sup>. The prevalence of IBS have been studied among study group and control group and in relation to age ,gender and type of TTH. CT and/or MRI done when it is indicated to exclude secondary causes of headaches.

**Inclusion criteria** : these are the diagnostic criteria of *Tension-type headache*<sup>24-27</sup>.

- A. At least 10 episodes fulfilling the criteria B-D.
- B. Headache lasting 30 minutes to 7 days
- C. Headache has at least two of the following characteristics:
  - Bilateral location
  - Pressing/tightening (non pulsating) quality
  - Mild to moderate intensity
  - Not aggravated by routine physical activity such as walking or climbing stairs

D. Both of the following:

-No nausea or vomiting

-No more than one of photophobia or phonophobia

E. Not attributed to another disorder.

The patients are subsequently subdivided in to *chronic type tension headache*(CTTH) when number of headaches per month more than 15 per months (180days/year)and *episodic type tension headache* (ETTH) when the number of headache episodes less than 15 per month (< 180 /year) <sup>6, 24,25</sup>.

### **Exclusion criteria**

The patients with features of migraine , transformed migraine, children less than 12 years of age\*\*, secondary headache, patients with chronic disorder like hypertension and diabetes were excluded in both control and study group.

### **Statistical analysis**

All data were pooled and analyzed in simple forms of tables with Statistical package for the social science (SPSS 15.0) , which is used in performing statistical analyses. The data were analyzed by means of person Chi-square tests with P value < 0.05 level of significance.

### **Results**

#### **Age and gender prevalence**

The age and gender distribution of patients in study and control group were shown in table 1 and 2. Among study group (total of 360 patients with tension headache), 200 (66%) patients were female and 160 (44%) patients were male (Female: Male ratio of 1.25:1); while among control (total of 200 healthy individuals); 116 (58%) were female and 84 (42%) were male (Female: Male ratio of 1.4:1). Although, there is clear peak prevalence among 30-50 years of age; but the difference is not significant statistically (P = 0.95) .

**Table 1:** Prevalence of tension type headache in relation to age and gender.

Age	12-20y	21-30 y	31-40y	41-50 y	51-60y
<b>Total</b>					
<b>Male</b>	5 (3.1%)	24(15%)	44(27.5%)	53(33.1%)	34(21.2%)
	160(44%)				
<b>Female</b>	7(3.5%)	38(19%)	51(25.5%)	59(29.5%)	45(22.5%)
	200(66%)				
<b>Total</b>	12(3.3%)	62(17.2%)	95(26.4%)	112(31.1%)	80(22.2%)
	360(100%)				

$\chi^2=1.38$

$p=0.85$

$df =4$

**Table 2:** Age and gender distribution among control group.

Age	12-20 y	21-30 y	31-40y	41-50 y	51-60y
<b>Total</b>					
<b>Male</b>	2 (2.4%)	13(15.5%)	32(38%)	22(26.2%)	15(17.9%)
<b>84(42%)</b>					
<b>Female</b>	3 (2.6%)	20(17.2%)	40(22%)	28(24.1%)	25(21.5%)
					116(58%)
<b>Total</b>	5 (2.5%)	33(16.5%)	72(36%)	50(25%)	50(25%)
					200(100%)

$$X^2 = 0.69$$

$$p=0.95$$

$$df=4$$

**\*\* headache under the age of 12 years were excluded in this study, because of the controversy about validity of adult International Classification of Headache Disorders criteria to TTH among children <sup>6</sup>.**

**Irritable bowel syndrome prevalence among tension headache versus control group.**

we found significant difference in prevalence of IBS among tension type headache group TTH (79.7%) versus control group (21%) ; P value was 0.0001 as shown in table 3.

**Table 3:** Prevalence of IBS among TTH group versus control group.

IBS	Positive	Negative	Total
<b>Patient</b>	<b>287(79.7%)</b>	<b>73(20.3%)</b>	<b>360 (100%)</b>
<b>Control</b>	<b>21(10%)</b>	<b>179(90%)</b>	<b>200(100%)</b>

$$X^2 = 248.9$$

$$p=0.0001$$

$$df=1$$

**Gender prevalence of Irritable bowel syndrome**

we found IBS cases is more common among women in both TTH group and control (62,7% and 52.4% respectively) versus men (37,3% and 47,6% respectively) ;but that was not significant ;  $X^2$  was 0.89 and p value was 0.346 as shown in table 4.

**Table 4:** Gender prevalence of IBS among TTH group versus control group.

Gender	Female	Male	Total
<b>Patient with IBS</b>	<b>180(62.7%)</b>	<b>107(37.3%)</b>	<b>287 (100%)</b>
<b>Control with IBS</b>	<b>11(52.4%)</b>	<b>10(47.6%)</b>	<b>21(100%)</b>

$$X^2_{0.89}$$

$$p=m0.346$$

$$df=1$$

**Distribution of IBS cases in relation to age .**

The peak age affected by IBS among TTH group were thirties and forties ( 29.6% and 28.6% respectively) while lowest was reported among twenties then fifties(20.9%

in both) . No case of IBS reported in teen age in both study and control group(excluded from analysis).The difference was not significant :  $X^2$  was 1.07 and p value was 0.785 as shown in table 5.

**Table 5** :Distribution of IBS cases in relation to age among TTH group and control group.

Age group	11-20y	21-30 y	31-40y	41-50y	51-60y	Total
<b>TTH with IBS</b>	-	60(20.9%)	85(29.6%)	82(28.6 %)	60 (20.9%)	287/360
<b>Control with IBS</b>	-	4 (19%)	6 (28.6%)	8 (38.1%)	3 (14.3%)	21/200

$X^2$  1.07

p= 0.785

df=3

### Is any difference in IBS prevalence in relation to TTH types ?

Interestingly, we found that IBS cases were more common among chronic TTH (93.3%) versus episodic TTH(72.9%) as shown in table 6 .The difference was highly significant ;  $X^2$  was 20.63 and p value was 0.0000056.

**Table 6:** Prevalence of IBS in relation to type of tension headache.

IBS TTH type	Negative	Positive	Total
<b>CTTH</b>	8 (6.7%)	112 (93.3%)	120 (100 %)
<b>ETTH</b>	65 (27.1%)	175 (72.9%)	240 (100 %)
<b>Total</b>	73 (20.3%)	287 (79.7%)	360 (100%)

$X^2$  20.63

p= 0.0000056

df=1

CTTH :chronic type tension headache

ETTH: episodic type tension headache

### Discussion

One of most common problem we face in our daily neurology practice is the headache especially tension type headache (TTH), which is the commonest among different types of headache<sup>3-6</sup>. The therapeutic approach to TTH is challenging in many cases and presence of comorbidity is very important from diagnostic and therapeutic point of view .Comorbidity is originally coined by Feinstein description in 1970<sup>31</sup>. He refers comorbidity to greater than coincidental association of tow condition in same individual<sup>13</sup>. Migraine comorbidity is well recognized<sup>13-17</sup> ; few studies were conducted about comorbidity of TTH<sup>18,19, 32</sup> .

**Age and gender distribution among TTH**

Although estimates of prevalence of TTH have varied widely, there is general agreement that TTH is more common in woman, with female to male ratios ranging from 1.04:1 to 1.4:1<sup>12,33</sup>; our study is consistent with that range and female :male ratio was 1.25:1. Unfortunately there is no study examine the prevalence of TTH in Iraq which is expected to be high because of socio-psychological influence of terrorisms. The headache under the age of 12 years were excluded in this study, because of the controversy about validity of adult International Classification of Headache Disorders criteria to TTH in children<sup>6</sup>. The age group distribution among our study group showed that TTH is a disorder of early adult life and middle with peaks between 20 and 60 ;this wider age range is more than that reported by others who estimate a peak of 30-50 years (middle life)<sup>4,8,10,11</sup>, this variation may be explained on basis of difference in case definition, sampling methods, or it is a real figures related to stress that affect wide age groups in our country in relation to sociopsychological elements; further multi center study is suggested to clarify the effect of these elements on prevalence, gender and age group variation in different areas of Iraq.

**Is the difference in prevalence of IBS among TTH patients versus control healthy individual is of clinical significance?**

The association between headache and psychiatric disorders is undisputed, with depression, bipolar disorders, and anxiety, and somatoform disorders being the commonest complaints<sup>34</sup>. Tension type headache TTH is mentioned as an associated disorder with fibromyalgia together with sleep disturbance, anxiety disorder, and depression<sup>18</sup>. Others mention TTH comorbidity as a part of dysregulation spectrum syndrome DSS with others entities including fibromyalgia, chronic fatigue syndrome CFS, migraine and restless leg syndrome<sup>21-23</sup>. DSS is defined as a common biophysical syndromes (mentioned above) that characterized by endocrine dysregulation and dysfunction that related to stress, but not all stress is necessarily psychological<sup>32</sup>. At the present time, no study examine comorbidity of irritable bowel syndrome (IBS) with TTH as separate entity; presence of such association have great impact in diagnosis and management of TTH patients.

**IBS and tension type headaches relationship**

**In this study, we observed two interesting observations ;the first is very significant high prevalence of IBS among patient with TTH in comparison to healthy individuals( 79.7% ,10% respectively) as shown in table 3. This is can be explained on the basis of shared underlying pathophysiologic aspects of IBS and TTH especially in relation to low platelet serotonin level and their clear association with emotional disorder and stress<sup>17, 28, 33,35,36</sup>.**

The platelet serotonin in patient with CTTH is reported by some studies to be lower than that in normal control<sup>35</sup>; but serotonin level in plasma may be elevated or lowered in few patients during ETTH<sup>36</sup>. In other side, there is no single unifying structural or physiological mechanism explain symptoms in IBS, several factors have been proposed including visceral hypersensitivity, abnormality of central pain processing(central pain facilitory neurons ;on-cells) and change in normal flora<sup>37</sup>. One theory describes serotonin fluctuation that over stimulates or suppress GIT motility in reaction to psychomotor events<sup>38,39</sup>, in similar way to TTH<sup>35,36</sup>. The relation between IBS and TTH remains complicated, and the important question raised; is these disorder (IBS&TTH) coexist together as part of comorbidity or DSS umbrella with shared common patho-physiological changes, or one precedes the other in variable time with

consequent development of other due to development or associations with reactionary psychological disorder ranging from simple stress to anxiety or depressive disorders as mentioned in many studies<sup>17,18,21,22,23</sup> ? to answer these questions definitely , further studies is needed to clarify this relationship .

*The second* interesting observation is the prevalence of IBS was significantly higher among CTTH versus ETTH (93.3% , 72.9% respectively) as shown in table 6 ; this is explained on the fact that CTTH reported to have more biochemical changes related to levels of platelet serotonin and gamma amino butyric acid (GABA)<sup>35,36</sup> , with more frequent association of CCTH patients with anxiety and depressive disorder<sup>17, 28, 33</sup> .

#### **Gender and age distribution of IBS among TTH patients**

The prevalence of IBS was more common in woman than in men with TTH (62.7% 37.3% , respectively);although the difference was not statistically significant as shown in table 4; but it can be explained on the fact, that both IBS and TTH are more common in women in most of studies for unknown reason<sup>28,33</sup> . The peak age affected by IBS among TTH group were thirties and forties ( 29.6% and 28.6% respectively) as shown in table 5 ; this is more or less not consistent with others who study the IBS in general population (but not among TTH patients) with predominant affection of people under age of 45 years and prevalence rose again in the elderly<sup>28,40</sup> ; at present no study estimate the age prevalence of IBS among TTH patients to compare that with our results; our results can be explained on basis of increasing stress and psychosomatic disorder among thirties and fifties among our people, where the people would have more life and family responsibilities with increasing stress that supposed to cause both TTH and IBS as mentioned in literature<sup>21-23</sup> .

In conclusion :at the present time, this is first randomized cross sectional comparative controlled study which showed significant comorbid relationship between TTH and IBS, the coexisting of tow disorders is very important in patient approach from diagnostic and therapeutic point of view. The strength of this association suggests common pathophysiologic mechanisms which needs further evaluation in a future studies.

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